# University of Birmingham

## Dr Nick Jones B.Sc (Hons), D.Phil.

Senior Lecturer

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### About

Nick Jones is a Senior Lecturer at the MRC centre for Immune Regulation.

Nick has a longstanding interest in dissecting the immune response to transplanted organs with a view to manipulating regulatory immune cell subsets and targeting T cell costimulatory molecules to facilitate the induction of tolerance and graft acceptance. He has published his work on the immunobiology of rejection and tolerance to foreign organ transplants in both transplant-related and general immunological journals which has been supported by major grants from Kidney Research UK, British Heart Foundation, Medical Research Council and the Wellcome Trust.

### Qualifications

- D.Phil. in Immunology (University of Oxford) 1996
- BSc (Hons) Biochemistry (University of Sussex) 1991

### Biography

Nick qualified with a BSc (Hons) in Biochemistry from the University of Sussex in 1991 before joining Celltech (an emerging biotechnology company) as a research associate. In 1993, Nick won an MRC studentship to study under the tutelage of Professor Kathryn Wood in the Nuffield Department of Surgery at the University of Oxford. Nick completed his D.Phil. in Immunology in 1996 on the mechanisms of tolerance induction by the intrathymic injection of alloantigen which was examined by Professors Don Mason and Bernt Arnold.

Nick was awarded a Senior Fellowship by Kidney Research UK in 2004 to continue his work as part of the Transplantation Research Immunology Group together with Dr Andrew Bushell and Professor Kathryn Wood at the University of Oxford. This enabled Nick to expand his studies on the utilisation of TCR-transgenic T cells to dissect the interaction and immune response of naive and memory T cells following the transplantation of foreign organ grafts. In October 2011 Nick joined the MRC Centre for Immune Regulation at the University of Birmingham as a Senior Lecturer.

To date Nick has supervised 2 M.Sc. and 7 PhD students and has presented his teams work at numerous national and international conferences. In addition, Nick or one of his team has won young investigator awards at the American Transplant Congress and the International Congress of the Transplantation Society, the Medawar medal and the Roy Calne award (twice) at the British Transplantation Society congress and the Promega Life Science Award at the British Society of Immunology.

In addition, Nick has completed a 2 year term as the councillor for Basic Science on the British Transplantation Society council.

### Teaching

**Teaching Programmes**

MBChB

BMedSc

MSc

### Postgraduate supervision

Nick is interested in supervising doctoral research students in the following areas:

- The role of invariant NKT cells in the immune response to transplants.
- Identification of different invariant NKT cell subsets for use as a cellular therapy to combat rejection
- Dissection of the mechanisms utilised by regulatory T cells to attenuate rejection
- Alloreactive memory T cell responses following transplantation

If you are interesting in studying any of these subject areas please contact Nick on the contact details above, or for any general doctoral research enquiries, please email: dr@contacts.bham.ac.uk (#contensis) or call +44 (0)121 414 5005.

For a full list of available Doctoral Research opportunities, please visit our **Doctoral Research programme listings. (#contensis)** .

## Research

**RESEARCH THEMES**

Transplant immunology, regulatory T cells, memory T cells, invariant NKT cells, rejection, tolerance.

**RESEARCH ACTIVITY**

**Background**

Transplantation remains the therapy of choice for end-stage organ failure however it's success depends on the effective prevention of transplant rejection. Currently this is achieved through the administration of potent immunosuppressive drugs that must be taken throughout the life-time of the transplant. Due to the non-specific nature of these drugs cancer immunosurveillance and immune responses to pathogens are also perturbed which can result in side-effects that are a significant cause of mortality and morbidity amongst the transplant patient population.

Therefore, one of the greatest challenges in transplantation is the discovery of ways in which rejection can be prevented without adversely affecting the beneficial functions of the immune system that serve to maintain health.

Nick is interested in exploring, at the cellular and molecular level, how different immune cells become activated and co-ordinately respond to a foreign organ transplant (allograft) with a view to developing strategies to specifically suppress anti-transplant responses.

**Invariant NKT cells**

NKT cells are a distinct subset of T cells, characterised by co-expression of surface markers for NK and conventional T cells. Most NKT cells express an invariant T cell receptor (TCR) with a V alpha14, J alpha18 chain in mice (V alpha24 in humans) and a heavily biased semi-invariant V alpha TCR chain, which recognise glycolipids presented by the monomorphic major histocompatibility complex (MHC) class I-like molecule CD1d. The most potent stimulator of iNKT cells is the glycolipid alpha-galactosylceramide (alpha-GalCer) which has provided an important tool for the identification and stimulation of invariant iNKT cells.

It has recently been demonstrated that although NKT cells have a key role in enhancing immunity they have also been found to facilitate the induction of tolerance in a number of models, including transplantation. However, how NKT cell responses affect adaptive immunity, serve to aid the induction of tolerance to allografts and whether these cells can be manipulated to reinforce tolerance have yet to be determined. Nicks lab have recently shown that iNKT cells are activated following transplantation but that such activation is not mediated through recognition of alloantigen by the T cell receptor. Rather iNKT cells become activated and secrete effector cytokine following activation by IL-2 secreted by activated conventional T cells. Nicks lab have also shown that different subsets of iNKT cells exist in different lymphoid tissues and that one subset is immunosuppressive whilst the other subset seems to induce a Th17 response that results in rapid graft rejection.

**Regulatory T cells (Treg)**

Regulatory T cells (particularly the $Foxp3^{+}CD25^{+}CD4^{+}$ Treg) are a subset of T cells with immunosuppressive properties that have been shown to be absolutely critical for the prevention of autoimmunity and the induction of tolerance to allografts in the experimental setting. Despite the wealth of data confirming their importance for immune regulation in numerous disease settings how they suppress the immune response to an allograft is incompletely understood.

Nicks lab have utilised techniques that allow the visualisation of alloreactive naïve or memory $CD8^{+}$ and $CD4^{+}$ TCR-transgenic T cells as they respond to allografts in the presence or absence of Treg. Employing such models Nick team has shown that Treg suppress alloreactive T cells in the peripheral lymphoid tissue. More interestingly, Treg also infiltrate allografts and limit the damage to the graft via an interferon-g dependent mechanism.

Defining the mechanisms by which Treg prevent allograft rejection will aid the development and implementation of novel therapies that allow the generation and manipulation of Treg to provide life-long tolerance to foreign organ transplants as well as result in refinements of assays to monitor the development and activity of such Treg in transplanted patients.

**Memory T cells**

Humans harbour significant numbers of pre-existing memory T cells (Tm) that can cross-react with donor antigens and influence the immune response to a transplant. Alloreactive Tm can also be generated after transplantation despite the use of immunosuppressive drugs and have been shown to have a negative impact on the survival of transplants. Moreover, it is now apparent that the presence of alloreactive Tm prior to transplantation can be detrimental to kidney allograft survival in clinical transplantation and the failure to induce tolerance to allografts in experimental models. Therefore, a clear picture is emerging that suggests that the success of conventional and novel experimental immunosuppressive reagents at promoting acceptance of allografts depends on the precursor frequency of pre-transplant alloreactive Tm and whether such cells can be adequately controlled with immunosuppression.

Indeed, Nicks lab has shown that memory T cells are far more resistant to the effect of numerous immunosuppressive drugs than are naive T cells. Furthermore, Nicks lab in collaboration with the Turka lab at the University of Pennsylvania showed that regulatory T cells are unable to control rejection elicited by memory T cells which may be due, in part, to the rapid rejection associated with enhanced memory T cell effector function.

Nicks work continues to try to understand the costimulatory molecule requirements of memory T cell responses to alloantigen and whether manipulation of Treg and iNKT cells may facilitate tolerance induction in this subset of T cells.

## Other activities

- Associate Editor, The Journal of Immunology (2009-present)
- Editorial board member, Transplantation (2003-present)
- Associate Review Editor, Frontiers in Immunological Tolerance (2010-present)
- Councillor for Basic Science, British Transplantation Society (2007-2009)

## Publications

Del Rio, M. L., N. D. Jones, L. Buhler , P. Norris, Y. Shintani, C. F. Ware, J. I. Rodriguez-Barbosa. (2012). Selective Blockade of Herpesvirus Entry Mediator-B and T Lymphocyte Attenuator Pathway Ameliorates Acute Graft-versus-Host Reaction. Journal of Immunology. 188: p.4885-4896.

Jukes, J. P., K. J. Wood and N. D. Jones. (2012). Bystander activation of iNKT cells occurs during conventional T-cell alloresponses. American Journal of Transplantation 12: p.590-9

Jukes, J. P. and N. D. Jones. (2012). Immunology in the Clinic Review Series; focus on host responses: invariant natural killer T cell activation following transplantation. Clinical and Experimental Immunology 167(1): p.32-39.

Wood, K.J., Bushell, A.R. and Jones, N.D. (2011). Immunological unresponsiveness to alloantigen in vivo – a role for regulatory T cells. Immunological. Reviews.

241:p.119-132.

Jones*, N. D., Brook*, M.O., Carvalho-Gaspar, M., Luo, S. and Wood, K.J. (2010). Regulatory T cells can prevent memory CD8+ T cell mediated rejection following polymorphonuclear cell depletion. European Journal of Immunology. 40: p.3107-3116 + In this issue highlights summary. *Joint first authors

Kinnear, G., Wood, K.J., Marshall, D. and Jones, N.D. (2010). Anti-OX40 prevents effector T cell accumulation and CD8+ T cell mediated skin allograft rejection. Transplantation. 90: p1265-1271.

Carvalho-Gaspar*, M., Jones*, N.D. Luo, S., Martin, L., Brook, M.O. and Wood, K.J. (2008). Location and time-dependent control of rejection by regulatory T cells culminates in a failure to generate memory T cells. Journal of Immunology. 180: p.6640-6648. *Joint first authors

Yang, J., Brook, M.O. Carvalho-Gaspar, M., Zhang, J., Ramon, H.E., Sayegh, M.H., Wood, K.J., Turka, L.A. and Jones, N.D. (2007). Allograft rejection mediated by memory T cells is resistant to regulation. Proc Natl Acad Sci U S A. 104: p.19954-19959.